

Related Efforts - Much effort has gone into designing fast computers by overlapping the micro-execution of program elements. Simultaneous operations on various elements of a computing load have been achieved through the design of special peripheral devices such as correlation processors and Fast Fourier Transform boxes. More flexible hardware devices may be designed using Clark's macromodules (ref. 15) or microprogrammed machines (ref. 16).

The coordinated use of clusters of small machines sharing memory and peripheral devices is being investigated by Bell (ref. 17, 18). This approach offers considerable long term potential when coupled to appropriate software capability. Software support must be available to effectively focus and manage such an array in a multi-user environment.

The proposed research in this grant does not have as its aim extensive research into computer architecture. Rather we will draw upon related developments in these areas (commercial and academic) as available for our specific medical applications.

Efforts are being made to provide support of remote computers by larger host systems. A number of manufacturers have available Assembly Language processors for minicomputers which run on larger hosts. IBM is developing a Distributed System Programming (DSP) system (ref. 19-20) which provides for communication of programs, data, and control information between a number of remote System 7 machines and a host. The announced capability of DSP is a 134 baud communication rate and no usable realtime priority structure in the host. The data rates of interest to this proposal are 3 to 4 orders of magnitudes higher.

### (c) Rationale

The underlying rationale of our approach to extended realtime problems in medicine is based on the concepts:

1. For problems involving large volumes of data or complex instrumentation and analysis procedures, the computer becomes a more powerful tool the more reliably, adaptively, and accurately it can perform necessary tasks without need of human supervision.
2. The integration of coordinated satellite machine capabilities with time-shared host facilities offers an effective and economical method for providing required computing resources among intensive users.

Automation - Most laboratory instrumentation data systems consist of the elements shown in Figure G-1 or some subset of those elements. In many cases human beings perform some of these functions directly in order to introduce adaptability and reliability. Inherent in the human performance of these tasks is a feedback situation where the results of an operation are evaluated in terms of "reasonableness" to verify the degree of success with which the task is performed and to

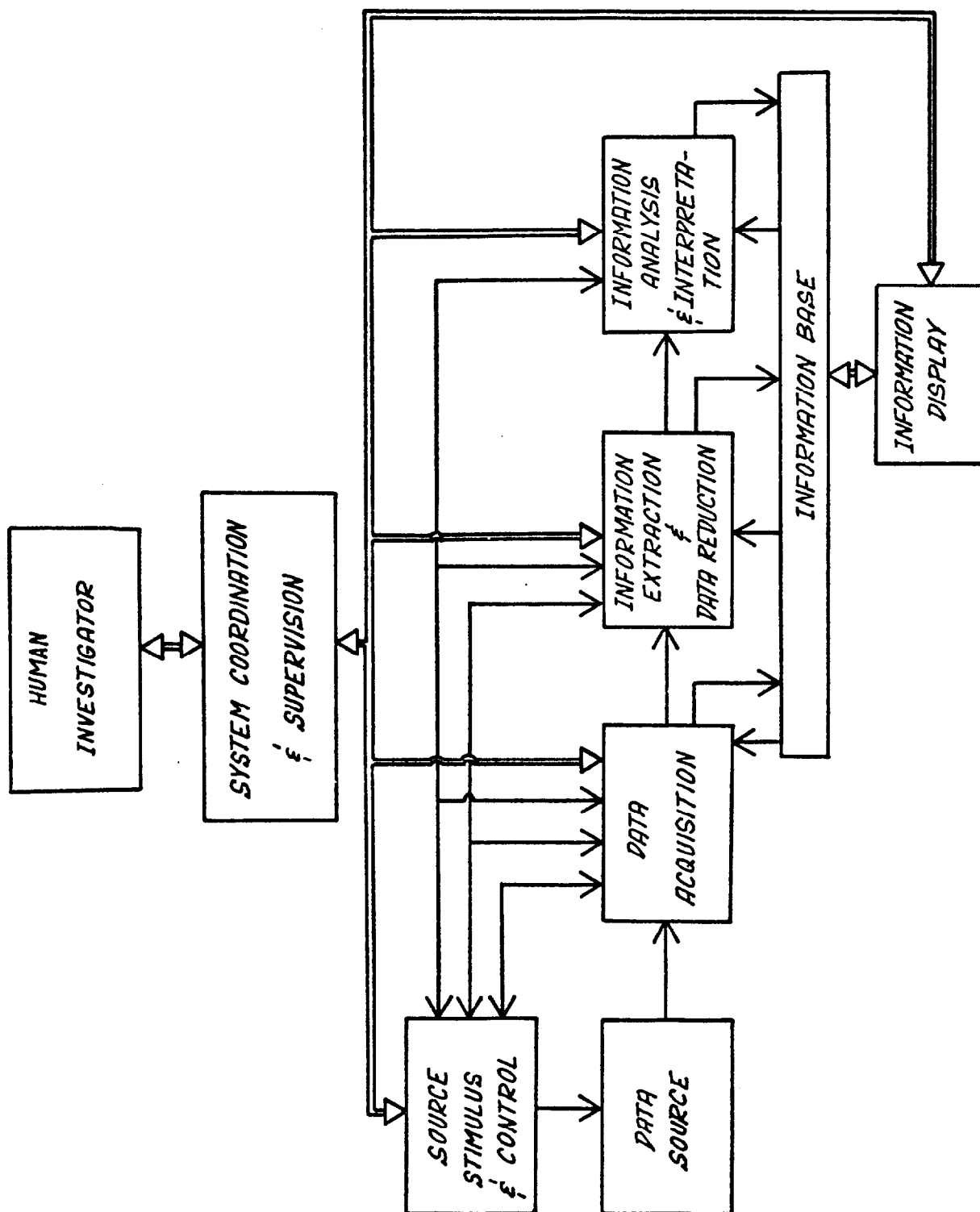


Figure G-1

modify the operation as required to optimize the result. Without this model for what constitutes an appropriate range for the process outcome, the human being would be no more reliable than the blind computer.

In situations where the human being cannot directly perform these functions, methods for automating the computer performance of such tasks must be developed. Such methods depend upon extending the underlying processing algorithms to include methods for adaptation, performance evaluation, and feedback optimization of processing parameters. Models by which the computer can judge and modify its performance can be based on physical models of the instrument or data source, heuristic models of the environment, or guidance from previously developed problem solutions. In the near term these models are defined by human control. In the longer term more autonomous computer organization of its problem domain will be required.

Computing Support - The use of remote and local satellite processors about a large host system with shared large core and peripheral equipment allows the economical expansion of parallel processing capacity and the efficiency benefit of sharing costly system resources. The general topology which we plan to use is shown in Figure G-2. This type of system can be constructed from available hardware and can take advantage of new developments underway at other locations. The satellite machines can be thought of as flexible building block processors which can be organized and programmed to support critical realtime projects while the main system acts to coordinate overall operation and provide less critical time-share, batch, and realtime service. These machines can be readily reconfigured by software to support various realtime tasks as needed and thereby are more efficiently shared among sporadic users. As necessary dedicated use of a satellite processor in a particular application such as a special instrument interface, is encouraged. Incompletely used and sharable resources are spread across a broader set of users.

#### (d) Methods and Procedures

Our approach to investigating extended realtime problems will be to set up a computing resource configured to meet anticipated extended realtime requirements and to select a set of problems in conjunction with a collaborator community with which to experiment with specific solutions. These problems will be selected to draw upon the expertise available in the Stanford medical and computing communities and to offer significant promise for application of these methods. It can be expected that the complement of problems under attack will evolve as successes and failures are encountered. In the longer term, attempts to generalize analogous solutions will be made. Significant progress remains to be made in the exposition of particular solutions,

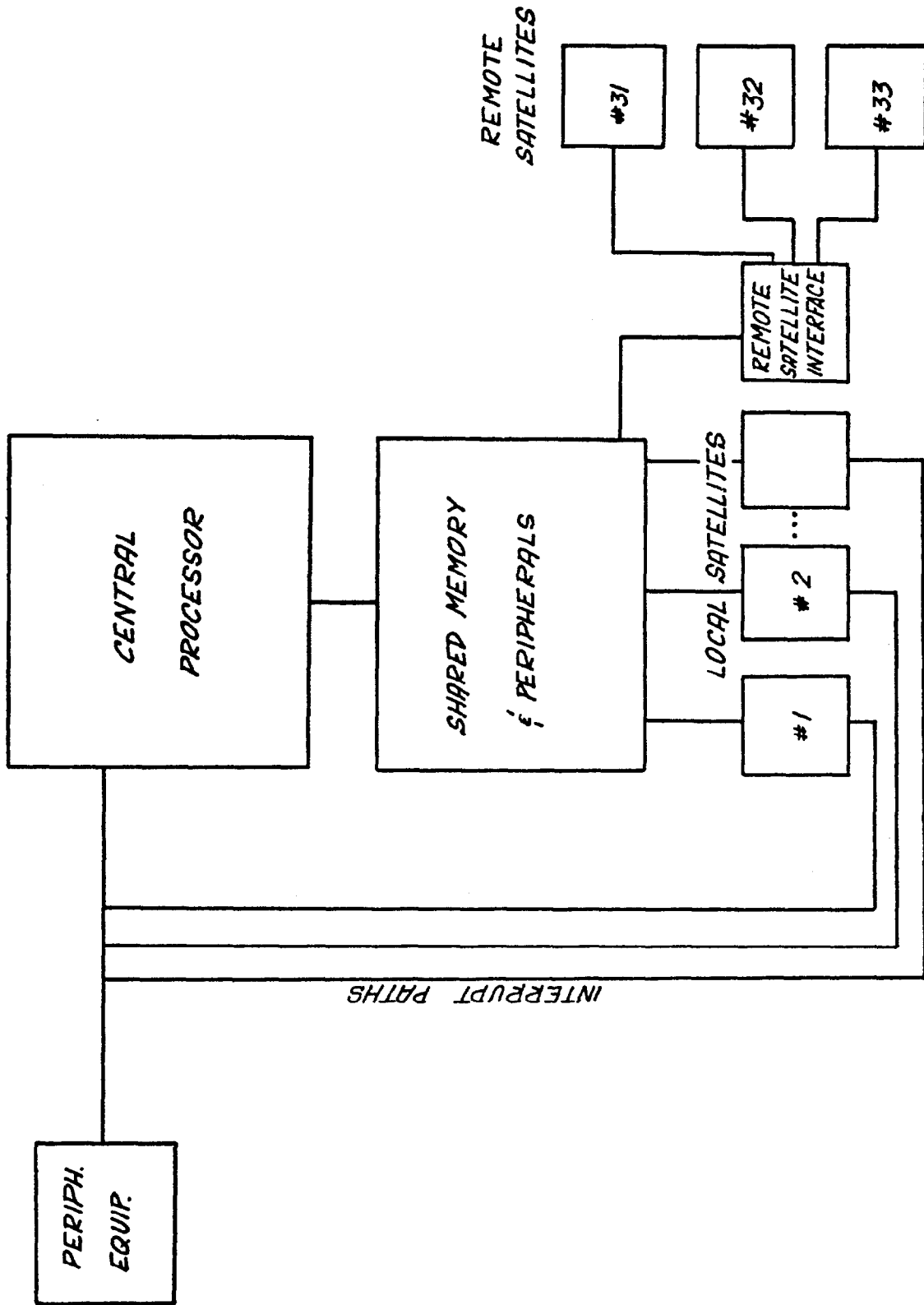


Figure G-2

however, before this will be possible. The initial complement of collaborative problems includes:

1. Harrison, et al.: Cineangiogram Analysis Automation.
2. Constantinou: Cineradiogram Studies of the Ureter.
3. Lederberg, Feigenbaum, Djerassi, Buchanan, Duffield, Smith: DENDRAL - Automated Mass Spectrum Interpretation.
4. Herzenberg and Levinthal: Cell Separator Automation.
5. Kopell, Roth and Pfefferbaum: Electroencephalogram Driven Stimulus/Response Studies of Drug Effects.

The backgrounds and proposed approaches to these research applications are contained in corresponding succeeding sections of this proposal.

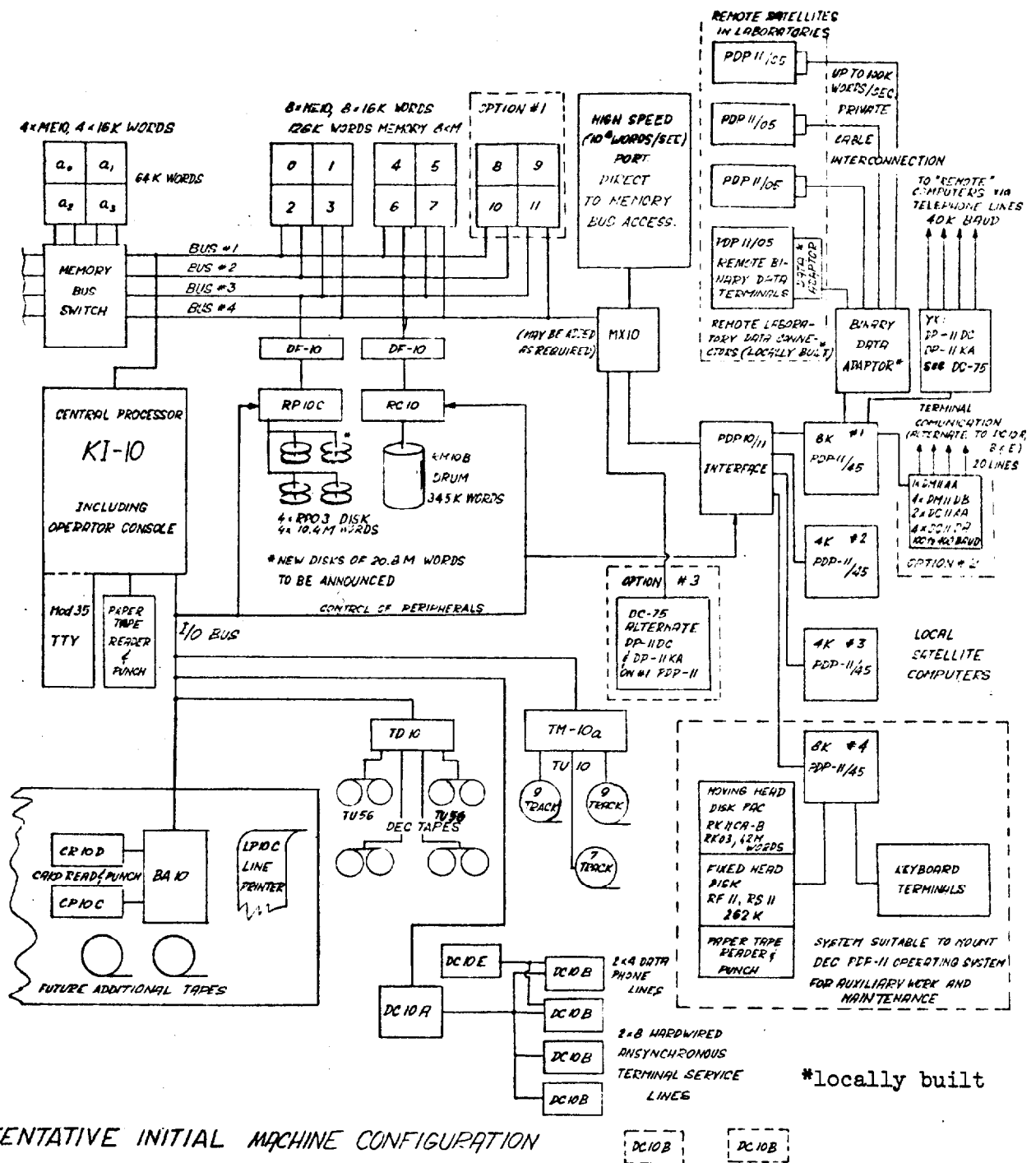
The computing resource will be built around a PDP-10 computer with a derivative of the PL/ACME time-share software system. The PDP-10 hardware configuration will be as shown in Figure G-3,\* with the following significant features:

1. The host computer allows state-of-the-art time-shared computing for system and program development as well as dedicated application to developmental realtime problems as required.
2. The direct memory access of the array of satellite PDP-11/45 processors provides for the experimental parallel processing support of intensive realtime applications in the time-shared environment.

The system will utilize the converted PL/ACME system as a base together with the developed satellite machine programming and communication system described in an earlier section of this proposal. Additional system software will be developed for interfacing and coordinating the satellite PDP-11/45 machines. It is expected that this software will evolve as application requirements dictate (see Figure G-4).

The satellite computers are considered to be available on call for a class of realtime users. The machines contain supervisory software which formalizes the PDP-10/PDP-11 interface by providing interrupt handling, intermemory transfers, program loading, program termination, and intermachine status and control monitoring functions. The satellites are allocated when not busy on the basis of a task list accumulated in the host machine posting requested user activity by sequence, type and priority. Each user application with access to extended realtime service will have available a set of routines which allow communication with the host monitor for posting of satellite tasks, priority control, on-going processing control and interruption, error and exception handling, input/output processing, and debugging facilities based on host and satellite language capabilities. Remote laboratory satellite

\*Identical to figure E-3. Repeated here for ease of reference.



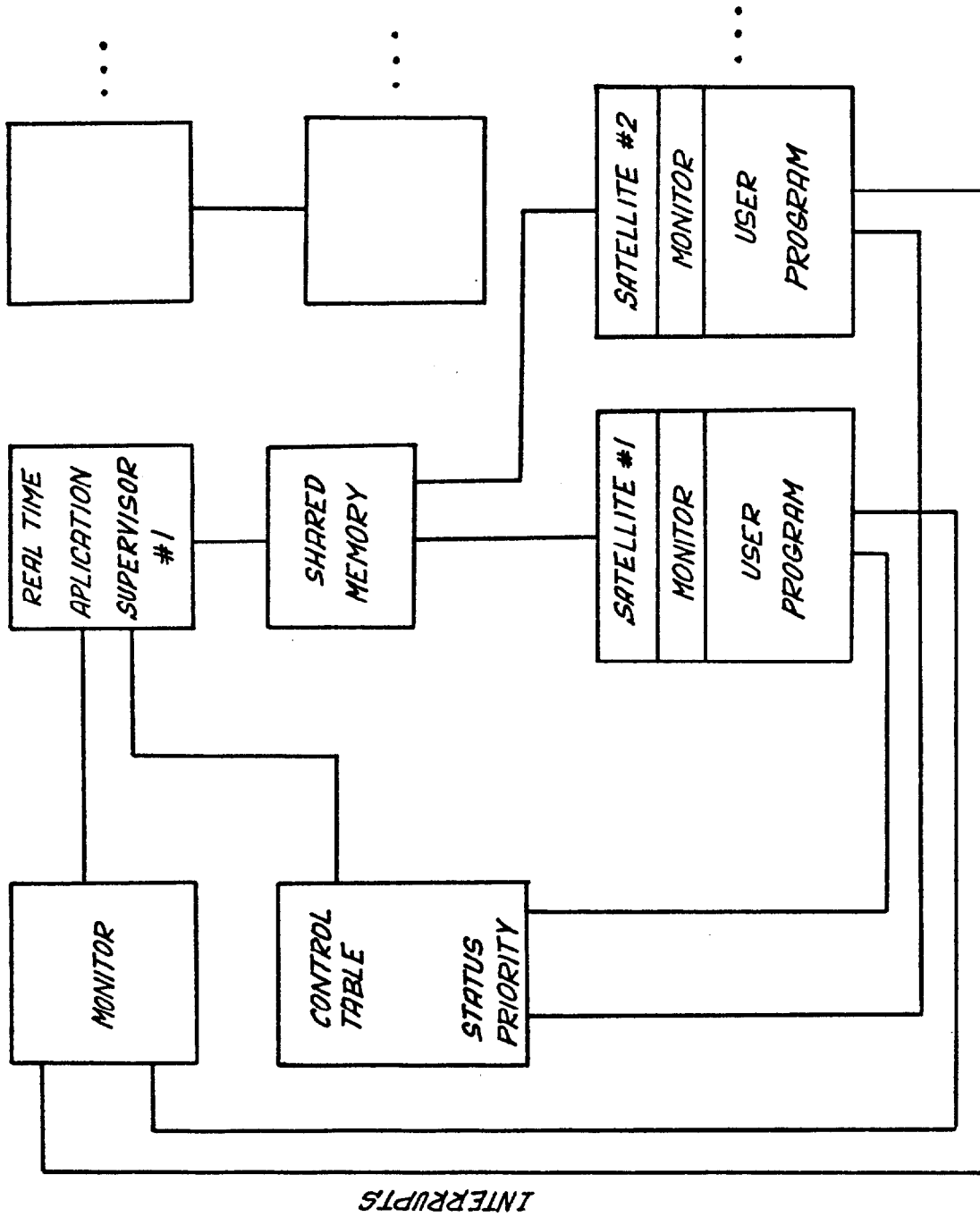


Figure G-4

computers will have similar support and responsibilities.

In general each realtime user has a supervisory driver which is responsible for job organization, synchronization, and coordination as well as outside user interactions. As each satellite performs specified tasks to completion it maintains updated status information on progress with the host system and upon completion of the task returns a completion status and frees itself for reallocation to the next highest priority task in the queue. The ability to service a community of users depends on providing enough satellites to accommodate scheduled loading within the adaptation constraints of each user.

(e) Significance

The development of reliable automated computer systems for dealing with complex and voluminous information in specific medical applications is important for a number of reasons:

1. Such tools augment capabilities for analysis and interpretation of increasingly complex measurements on biological systems.
2. Such tools provide a means for collecting quantitative data from large populations establishing statistically sound baselines for testing research hypotheses.
2. Such tools are an essential element to the routine delivery of preventative health care to large populations.

The significance of the associated research applications we have chosen **speaks for itself**. Clearly one must not expect the computer to replace human capabilities but to augment and extend them. Progress has been made on a few problems to date and progress must be made on many more fronts.

(f) Collaborative Arrangement

The essence of the proposed approach to extended realtime research is to select a specific set of significant problems to provide a basis for more general solutions. These specific applications draw upon the expertise of the collaborators named above.



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(3) PL/ACME on a PDP-10

The PDP-10 systems as provided by DEC contain an excellent timesharing system with its memory allocation, support a variety of languages and have an adequate file system.

A service that ACME has provided is a language and a support system that has a number of features not included in the DEC processors:

- (a) A language that conveniently handles both numeric and string data.
- (b) The capability to alter programs in terms of source statements at any time, including execution.
- (c) The capability to carry out all debugging, including interruption, inquiry into state of variables or system change of variables, and continuation from such points, in source program formats.

These points have made ACME a useful tool for non-computer specialists in medical research.

Most of these features are part of the compiler and the execution time support provided through availability of symbol table, controlled linkages, etc.

We therefore would like to put a PL/ACME language processor on the PDP-10 if such a machine is obtained for Stanford. Before starting this project, we will look for other options to provide PL-type language support on the PDP-10. The language processor should be useable on other machines of similar type and configuration. We will seek other PDP-10 users of PL and form sharing efforts on language extension.

The work is simplified by the fact that major portions of PL/ACME are written in FORTRAN and that the compiler does not generate directly 360 machine language. It generates specification to a macro assembler which produces the detailed code.

It is DEC's impression that their new FORTRAN compiler will materially assist this conversion effort.

A number of decisions will have to be made regarding byte size and other parameters. ACME's byte size is 8 bits, determined by the IBM hardware; DEC hardware is flexible. Their software normally prefers 7, but their COBOL uses 6, as do their peripheral devices in standard mode.

The estimate of the required conversion effort that follows was made by the ACME staff members based on discussions with DEC to clarify PDP-10 system capabilities and services. DEC made no direct examination of ACME code in responding to our general queries.

The following assumptions were made in arriving at the estimate:

- (a) Indicated man month requirements assume uniform concentration on the problems of conversion. Competing demands on personnel time will introduce inefficiencies and increase calendar time required.
- (b) The staff will consist of qualified systems programmers familiar with the PL/ACME system augmented by member(s) previously familiar with the PDP-10 system.
- (c) No attempt will be made to extend PL/ACME capabilities in the conversion effort. Reprogramming will include taking advantage of existing PDP-10 capabilities including monitor control of time-share allocations, core swapping/hardware relocation or paging, and a file system which on the surface is similar to that currently used by ACME (there may be differences in security and integrity provisions).
- (d) The new FORTRAN compiler being designed by DEC will be efficient, compatible with language standards, and allow efficient provision for extended capabilities such as logical operators, byte manipulation, and binary shifting.

The following are the conversion estimates for a PDP-10:

<u>System Function</u>	<u>Man-Months</u>
1. Statistical programs	2 mm
2. PL compiler	12
3. Error messages/processing	1
4. Execution time excluding I/O	6
5. File System	6
6. Run time I/O and text editing	6
7. LISP compiler	0
8. Miscellaneous	1
9. SYSI. FORTLIB (FORTRAN library)	1
10. Plotting routines	2
11. Core management	1
12. Realtime support (configuration dependent)	3
13. System control	3
14. Terminal handling	1
15. Assembly utility	1
	<hr/>
Sub Total	46 mm

In addition to converting program code, provision must be made for planning the conversion details, learning the new computer and monitor system, and assistance to users in file conversion:

16. System education (4-5 people @ 1.5 mo/person)	7 mm
17. Conversion planning	12 mm
18. User file conversion aids	4 mm
	<hr/>
Sub Total:	23 mm
Grand Total	69 mm

In the above estimates no provision was made for project management, project service, or operations personnel time as well as hardware costs. Additional software effort will be involved in building accounting routines for a new machine/environment. More significant and user dependent will be some user effort to convert data files to a new word length system. For files of uniform format (numeric or alphameric (text)), conversion can be automated. For mixed files the user must be involved to define the formats of the data. Provision is made in the above estimate to generate file conversion program aids based on user format specifications.

The LISP conversion problem is in essence ignored above based on the following. No adequate LISP capability currently exists on ACME. The LISP 1.5 batch processor currently used on the 360/67 has a counterpart on the PDP-10 which requires minimal conversion of programs using conventional LISP functions. According to B. Buchanan, some DENDRAL LISP code includes special functions written in LAP (a LISP assembly language) which will require conversion. This code is not voluminous and some will benefit from conversion and/or redesign.

b. Collaborative Research and Development

(1) Predictive Modeling of Cardiovascular Function Utilizing X-Ray and Ultrasonic Imaging Techniques - prepared by Donald C. Harrison

(a) Problem Statement

Cardiovascular disease continues to be the leading cause of death in the United States and in most developed countries, even though significant research into the prevention, diagnosis, and treatment of cardiac conditions have provided much insight during the past several decades. Coronary artery disease (CAD) accounts for more than 50% of all deaths in the United States and between eight and ten million people are estimated to have symptomatic CAD at the present time. Untold more millions have latent CAD which has not yet been detected. CAD frequently does not involve the muscle of the heart wall symmetrically and in fact, typically, is segmental in nature leading to localized areas of dysfunction with areas which are dyskinetic, akinetic, or dyssynchronous in their contraction patterns. All of these abnormalities may occur in the same heart and in general, can be correlated with a decrease in coronary blood flow to the specific segment of myocardium. In order to determine which patient should receive medical or surgical therapy for CAD, and whether or not segments of wall should be removed in specific patients, it is important to define in quantitative terms the areas of abnormal contractility and their severity.

Patients with valvular heart disease also may have localized abnormalities of muscle contraction in their heart wall. In determining whether or not the valve damage is primary, thereby requiring surgical therapy, or whether it is secondary to the abnormal muscle function, sophisticated studies such as cardiac catheterization and specific angiographic procedures must be performed. Data which are obtained from these complex procedures are in many instances inadequate to make a precise assessment of muscle function. Thus, our overall desire is to develop techniques which will permit a better assessment of ventricular performance, first by using the invasive techniques of cardiac catheterization and angiography now available, but providing improvements for analyzing signals. Secondly, we wish to develop new techniques, primarily using ultrasound, which will not require cardiac catheterization and angiocardiographic procedures for defining precisely cardiac muscle function.

Computer technology has been applied successfully in order to permit more accurate assessment of cardiac function in recent years. Computer techniques for monitoring the electrical and mechanical performance of the heart in a number of disease states have been developed in the Cardiology Division at Stanford (1-4). Dedicated small computers have been used for these purposes and the programs for determining pressure and flow relationships in patients undergoing cardiac catheterization have been developed by the Cardiology Group at Stanford (1-3). These functions are now performed by a dedicated mini-computer operating in a real-time mode during much of the day. In addition, the software for monitoring electrical and pressure-flow relationships in patients following acute heart attacks is presently being developed by the Cardiology Group. The basic software package for this dedicated mini-computer has been developed, and validation of these computer programs is now in progress.

A technique for video image analysis obtained when patients are undergoing angiocardiographic procedures has also been developed by the Cardiology Group (4-6). Furthermore, techniques for monitoring the coronary blood flow as it is partitioned to various muscle segments in the heart has been developed using a gamma camera for counting radioisotopes after the injection of gamma emitting isotopes into the coronary arteries. Individual patients undergoing cardiac

evaluation or treatment at Stanford may well have tests or procedures which are analyzed by all three dedicated mini-computers now operative in Cardiology. Since all calculations are now being carried out by mini-computers which are not tied together in any network, the special calculation and integration of data from any specific given patient is not possible without the use of a larger computer system. The Cardiology Division desires to utilize the proposed research computer system in order to develop more sophisticated techniques for studying the function of the heart, and to develop techniques which can be applied widely for choosing the appropriate diagnosis or treatment of specific patients with cardiac disorders. The specific problems which we wish to solve are as follows:

1. To diagnose the presence of disease of the cardiovascular system and to quantitate its severity utilizing data being generated by the several dedicated mini-computers monitoring cardiovascular performance. The ability to perform multiple sophisticated calculations on these data which can be integrated from several dedicated mini-computers in Cardiology will provide a basis on which to define heart muscle and hydraulic pump function in a more precise manner.
2. Utilizing the X-ray image processing techniques to improve analysis of the hydraulic function of the heart, it should be possible to estimate and detect segmental abnormalities in function. Clearly, much can be learned from studying the geometric changes in the heart wall during contraction which can supplement the pressure-flow relationships which we are now using for analyzing function.
3. To integrate the pressure-flow-volume and geometric changes for the entire heart and for the small segments of the wall representing small areas of muscle dysfunction or necrosis which may be important for overall cardiac function.
4. To develop non-invasive methods utilizing ultrasound techniques as a substitute for angiography which will permit screening of patients with suspected cardiac function abnormalities without subjecting them to the considerable risk of cardiac catheterization and angiographic techniques. It is also possible that these ultrasonic techniques can be applied in non-hospitalized patients, thereby decreasing the cost of screening significantly.
5. To follow the course of cardiac disease by studying in quantitative fashion the changes in function in relationship to pressure flow, volume, and geometry as a natural history of a disease process unfolds.

(b) Background

During the past two decades, pressure measurements in the various chambers within the heart have been the primary method for determining dysfunction. Transducer systems for analyzing the cyclic changes in pressure have been available for several decades, and abnormalities of valve function and muscle function are reflected in changes in systolic pressures, diastolic pressures, and the rate at which pressures are developing. During the past two decades measures of total flow during the cardiac cycle have been developed and used together with pressure measurements to provide a more sophisticated technique to analyze the overall hydraulic pumping function of the heart. Recently techniques for measuring volume changes throughout the course of a cardiac



cycle have been developed at Stanford. Video images are stored on a video disc after the injection of radio-opaque media into the cardiovascular chambers. Then utilizing a light-pen for drawing the images on a video screen and transmitting the coordinants from the light-pen to a computer, has provided a basis upon which ventricular volumes could be determined throughout the cardiac cycle once geometric formulae for the changing ventricular shapes were developed. This technique is tedious, requires a human interface and does not provide high resolution. In an attempt to improve these methods of determining ventricular volume, techniques for videodensitometry which have been developed at the Mayo Clinic (7) and in Dr. Heintzen's laboratory in Germany (8) are now being planned for cardiology laboratories. Videodensitometry requires that computer processing techniques be developed to recognize borders and that the movement of these various borders be followed throughout several cardiac cycles while the ventricular chamber is filled with radio contrast material. These techniques offer great promise for studying the geometric changes which occur during cardiac contraction and for defining the changes which occur segmentally in patients with CAD. However, even these sophisticated techniques require cardiac catheterization and angiography.

Recently the use of reflected ultrasonic waves from the moving wall of the heart has been accomplished in a number of centers throughout the United States. These techniques offer promise for a non-invasive method to study heart function. Using these reflected ultrasound techniques, it is possible to determine specific patterns of wall motion for a given area of the heart. Unfortunately, it is difficult to locate precisely these areas and to make certain that one can focus the ultrasonic beams on a specific area throughout the course of a cardiac cycle or throughout several cardiac cycles. The development of new and multiple ultrasonic transducer systems may provide an opportunity to look at more than one area of movement in the heart wall. With multiple transducers, computer processing of ultrasonic data becomes essential. In the Cardiology Division at Stanford we have developed a rapid A-D conversion technique for computer processing these ultrasonic signals, and have developed tracking programs and pattern recognition techniques. At present our progress is limited without access to a large computer which can receive high data input, store it for later calculations and then display it graphically. Multiple transducers are now being developed and with them it should be possible to analyze more than one area of wall motion in a particular cardiac cycle. Such transducer systems are available now, but their use is delayed due to the general inability to process the accumulated data. Computer techniques for handling the large volume of data are now being considered and will require access to a large computer with extensive core, disc storage, and sophisticated graphic outputs.

(c) Rationale

The specific rationale for proposing the use of the large research computer facility at Stanford at this time is as follows:

1. The Cardiology Division has made a step-wise approach, utilizing dedicated small computers to measure cardiovascular functions and follow them in quantitative terms. Computer techniques for analyzing pressure and flow signals have already been developed and initial applications utilizing a human interface have also been made for video image processing.

2. Analysis of cardiac contraction patterns, segmentally, necessitates high video frame rates with video image processing of each frame. It appears that videodensitometric methods utilizing techniques for determining border movement for various segments of muscle throughout a cardiac chamber are essential to provide quantitative data.
3. Sequential analysis of discrete areas of ventricular wall motion so that disease which alters the function of a particular segmental area of the heart can be detected. The nature of coronary artery disease is that segmental wall damage is almost always the way in which ventricular function is altered.
4. Advanced technology in ultrasonic transducers is now being developed. Dr. Richard Popp of the Cardiology Division at Stanford and Dr. James Meindl of the Integrated Circuits Laboratories in the Stanford Electrical Engineering Department have been working on such multiple transducer systems. Clearly the ability to sense the signal from these transducers and to activate one transducer at a particular time during the cycle and analyze from that transducer will require large and sophisticated computer installations.

It is with these rationales in mind that the Cardiology Division desires to participate in the development of the research computer facility at Stanford.

(d) Methods and Procedures

Several specific procedures to improve definition and provide quantitation of cardiac function are planned.

1. X-ray Image Processing - New image processing techniques will be developed. The goals and methods for accomplishing this particular research project are:
  - a. To outline the opacified heart chamber after the images are recorded on either X-ray film or on a video disc. Recording will generally be made at 30 frames/sec. for delayed analysis. Several techniques for border definition will be attempted. Gray Scale analysis techniques utilizing scan methods for digitizing data along lines on the film or video scan will be one of the methods attempted. A film scanner will be necessary and will need direct computer control.
  - b. Since biplane opacified images will be processed, three dimensional geometric displays of ventricular contraction will be developed. A promising technique of cartooning video images in three dimension has been developed by the Cardiology Division in association with Dr. Harold Sandler at NASA Ames Research Center.
  - c. Models of the normal contractile patterns for ventricles will be developed. Changes expected during various parts of the cardiac cycle can then be predicted by the computer and only those areas in which the contractile pattern differs significantly from normal will be studied in detail. This ability for the computer to focus the analysis on areas of abnormality by feed-back mechanism excludes extraneous data from being digitized and analyzed. This technique will permit a much more adequate use of the sophisticated computer technology and a great reduction in the volume of data handling necessary when high frame rates over many cardiac cycles are examined.

- d. Segmental analysis of various portions of the heart wall motion will be possible using these computer techniques.
- e. Data on pressure and flow accumulated simultaneously will allow precise calculation of muscle function in terms of force-load-velocity of contraction and will permit pressure-volume loop displays. Graphic display of the computed data will be essential for these calculations.

In the understanding of isolated muscle segment function it is important to ascertain the relationship between force developed and velocity of wall motion in a specific segment. This should provide a basis for understanding the hydraulic relationships developed in the pumping heart as a whole on the basis of individual segment analysis. Thus, it will be possible to develop pressure-volume loops for the analysis of overall cardiac function. The quantitative determinations of overall function can then be related to normal expected patterns. Predictions of change in cardiac performance, based on removal or alteration of contractility of a given segment, can then be made with precision. This will perhaps lead to a better understanding of the function of isolated segments of ventricular muscle and how these are affected by disease and the treatment of that disease by either medical or surgical means.

## 2. Ultrasonic Image Processing

It is the developmental plan of the Cardiology Division to utilize information concerning cardiac function obtained by contrast angiography to validate and provide a data base for the newer techniques of ultrasonic image generation and processing. Detailed measures of ventricular contraction utilizing ultrasonic image processing techniques appear possible in more than one dimension. Several transducers may be used to reflect the movement of the heart wall in three dimensions.

During the first year of the proposed grant we plan to develop better techniques for digitizing ultrasonic data and to improve our methods for tracking ultrasonic signals in real-time utilizing digital computer techniques. In addition, during this period of time the development of multiple transducers on a hemispherical array will be completed in collaboration with Dr. James Meindl in the Integrated Circuits Laboratory at Stanford. Computer software for activating one transducer and recording from it for a short period of time and then sequentially activating other transducers so that three dimensional ultrasonic display of ventricular wall motion can be made will be developed utilizing the PDP-10 computer system proposed.

Border definition recognition, and sequential motion analysis can be predicted for normal hearts and deviations from normal can be highlighted by activating the appropriate transducer in the hemispherical array for systematic data accumulation throughout cardiac cycles. This should permit the development of non-invasive techniques for studying wall motion in patients who have only latent heart disease and are not yet symptomatic. Mass screening techniques with physiological documentation will be required once these ultrasonic scanning techniques have been validated. It seems likely that ultrasonic techniques can replace the invasive radiographic methods now required to analyze wall motion in quantitative terms and relate this to pressure and flow data.

### 3. Small Computer Integration

The Cardiology Division wishes to transfer the data analyzed by the small dedicated computer systems in the cardiac catheterization laboratory, in the monitoring unit, from the gamma camera, from the electrocardiographic laboratory and from a gas chromatograph into the large research computer file automatically. Currently the integration of these data and performing calculations with interrelated data from the several systems can only be done manually. To this data pool for sophisticated analysis we plan to enter the X-ray image processed data, the clinical data, and the data from the operating rooms. Once these data can be analyzed in detail, highly sophisticated diagnoses, prognoses, and predictive estimates for specific patients with a variety of cardiovascular diseases can be made.

From the monitoring unit on the cardiology ward specific cardiac arrhythmias can be detected and their frequency quantitated. These arrhythmias are treated with drugs which can be measured precisely by gas chromatography. The level of the drug can be related to its effect in many patients. Control of its administration can be achieved by relating the frequency of arrhythmia to blood level of the drug used for treatment. We wish to experiment with computer control of drug administration in these specific circumstances.

#### e. Significance

The significance of the above proposed analyses of cardiac function is as follows:

1. To understand better the physiologic interrelationships between changes in coronary blood flow, segmental muscle dysfunction and overall hydraulic pumping abnormalities in the heart of patients with significant cardiac disease. It will be essential to study isolated muscle function in a segmental distribution and to integrate the pressure-flow-volume and geometric measures of ventricular performance.
2. To choose appropriate medical or surgical therapy for the large numbers of patients presenting with cardiac disease based on quantitative determinations of abnormalities in cardiac function.
3. To evaluate sequentially in quantitative terms the results to either medical or surgical therapy in these patients.
4. To develop and improve non-invasive techniques which will provide all of the information necessary to analyze heart function in quantitative terms. These approaches may later lead to mass screening techniques for latent disease.

Clearly, if the objectives outlined above are met successfully by the research computer facility, they will become daily operational activities for cardiologists. In this instance the programs developed could be moved to the utility machine or to small dedicated computers of this type now used by the Cardiology Division. Specifically, it is planned after each of these techniques are developed and validated they will be moved to the Medical Center utility machine.

## f. Relationships

The Cardiology Division works with a number of other units within the Medical School and in the Undergraduate University. In order to utilize the proposed computer facility as has been described, it is essential that these relationships be maintained and increased. Presently the following interrelationships are maintained by the Cardiology Division as they are operative in relationship to this proposed computer grant.

1. Cardiology Division is directed by Dr. Donald C. Harrison, Professor of Medicine, Stanford University School of Medicine, who has during the last five years emphasized research for adapting computer techniques for cardiologic diagnosis and treatment. Dr. Robert Stenson will be joining the Cardiology Division as Assistant Professor of Medicine. He has an extensive background in computer sciences and in cardiology and will direct the computer research operations for the Division. Dr. Edwin Alderman and Dr. Richard Popp are both working with video image processing--Dr. Alderman with angiographic methods and Dr. Popp with ultrasonic techniques. They both are working with a number of collaborators and postdoctoral trainees on projects which will relate closely with this computer technique development. Mr. William Sanders, who has worked with the Cardiology Division for two and one-half years as the Chief Programmer, will direct the programming efforts and will work as a liaison man with the overall computer staff of the proposed central computer facility. During the past year two graduate students from Electrical Engineering, Mr. Michael Hirsh and Mr. Patrick McClure, have worked in association with Mr. Sanders. At the present time in Cardiology two Hewlett-Packard computer systems are operational on a day-to-day basis. The Cardiology Division has also been approved for an M.D. training program in computer sciences. This will be carried out in association with Dr. Edwin Parker of the Communications Department and the Computer Sciences Department in the Undergraduate School at Stanford. Furthermore, the Cardiology Division is presently negotiating with Hewlett-Packard for another 2100 computer system which would then give the Cardiology Division three small dedicated computer systems to be integrated into the larger proposed Research Computer network.
2. NASA Relationships - Dr. Harold Sandler, Head of the Biotechnology Group at NASA-Ames Research Center is one of the pioneers in angiographic methods in studying ventricular geometry and cardiac function. The Cardiology Division has worked closely with Dr. Sandler and at present all of his clinical work is performed in our cardiology laboratories at Stanford. NASA has also supported an ongoing project for the past five years at Stanford to develop better methods for analyzing ventricular performance.
3. Integrated Circuits Laboratory - Dr. Richard Popp is working closely with Dr. James Meindl in designing new arrays of ultrasonic transducers. This work is at an early phase at the present, but plans are being made for more than one transducer mounting so that several segments of wall motion may be studied in the same heart.
4. Communication Department - Dr. Edwin Parker of the Communication Department has agreed to work with the Cardiology Division in a training program for medical scientists in the application of computer techniques for data handling and analysis. Such a program has been approved by the Study Section of the National Library of Medicine and should be activated in the year 1972.

5. Artificial Intelligence Group - Numbers of individuals working in the Artificial Intelligence Group have worked with image processing techniques which will be complementary to the plans in Cardiology. Tom Rindfleisch, Dr. Elliott Levinthal, and Dr. Bruce Buchanan of this group have participated with the Cardiology Division in planning the image processing techniques to be utilized. Professor Lederberg and Dr. Levinthal are on the Mariner 9 TV Experimenter Team. In this capacity, Dr. Levinthal has headed the Data Processing Task Group which has had the team scientific and policy responsibility for the very large image processing computer requirements for this mission (ref. 31).

Mr. Thomas Rindfleisch, when he was at the Jet Propulsion Laboratory had the responsibility for the implementation of this system. There is thus the opportunity to benefit from these space-related experiences in image-processing.

In addition, Dr. Buchanan is closely related to the M.D. Computer Science training program of the Division of Cardiology. These inter-relationships will provide high level computer consultation for the Division of Cardiology as the step-wise plan to utilize the proposed research computer facility above unfolds.

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2) Digital Computer Processing of Cineurographic Images of the Urinary Tract. - prepared by C. Constantinou and T. Stamey

(a) Problem Statement

Due to the expanding sophistication and specialization of the clinical urologist, the specific need for computer aided quantification and documentation of X-ray images is becoming increasingly urgent. Thus, with the routine introduction of cinefluoroscopy as a dynamic mode of visualization of the urinary tract, the quantity and quality of information available to every day diagnostic procedures has greatly increased. At the same time, the objective evaluation and quantification of this information remained in the cognitive mind of the radiologist who is asked to provide a larger volume, accurate measurements, and at the same time, maintain a consistent diagnosis. To this end, some information is available to the urologist from static X-ray films as measured by the radiologist. This information includes renal size, parenchymal thickness, calyceal geometry, pelvic and ureteral dimensions and can be reasonably abstracted and documented manually by measurement. But a living system is not static and therefore dynamic studies, using cinefluoroscopy, have been organized to view the kinetics of peristaltic flow, retrograde reflux, and dilation, in the ureter on film. This effort has proven very useful for first order visual evaluation by the urologist but has inherent limitations in terms of quantitative data that can be abstracted in a manner analogous to the static X-ray measurement.

The broader application and objective use of these dynamic studies is therefore limited due to the vast amount of work and calculations required for the determination of even the most basic parameterization of any of the kinematic constants. It is in this area of dynamic interpretation of extended cinefluoroscopic studies with its plethora of potentially valuable information that this program addresses itself now.

The overall objectives of this proposed program is the development of the computational capability to greatly increase the informational content of intravenous pyelographic film. It is expected in this way that an extensive determination of the dynamics of flow of the upper urinary tract under physiological and pathological conditions can be made. Specifically, the following parameters will, for the first time, become available in a simultaneous measurement from the computer processed film:

1. Volume, dimensions, and direction of propagation of the discrete urine bolus.
2. Speed of peristaltic transmission and frequency characteristics of a group of contractile waves.
3. Spatial separation of retrograde peristalsis and reflux under various conditions of flow.
4. Accurate documentation of time varying changes of above in disease situations where there is known progressive deterioration in the lower ureteral tract.



5. Correlation of these changes with the geometry of the upper tract and kidney.

The direct benefits of this integration and quantification of parameters would significantly enhance the informational content of pyelography for the urologist and radiologist. At the same time the underlying mechanisms of obstructive uropathy would be quantitatively evaluated and compared to normal physiological pressures.

(b) Background.

In clinical urology, the transport of urine from the kidney to the bladder is visualized radiographically by the injection of radiopaque contrast media into a vein and observing the outline of the calyceal walls and the excretion patterns of the ureter during peristalsis. This diagnostic procedure is termed intravenous pyelography and frequently performed in most hospitals. The dynamic nature of the transport of urine in the ureter is enhanced when observations are made continuously through a fluoroscope to visually trace the path of the contrast labelled urine along the entire length of urinary tract. Thus, the anatomical outline, from kidney to bladder, is illuminated and obstructive or restrictive pathways can be observed. The amount of information thus extracted is substantially increased when a permanent record of the flow patterns is documented on cine film or video tape, and subsequently examined at slower speeds. At that time, retrograde flows can be seen together with a host of other physical phenomena characteristic of a diseased kidney, ureter, or bladder. The informational content of this visual examination is presently limited to a qualitative description of size, shape, position, and primitive motion of the ureters. Films or tapes resulting from these studies are stored and subsequently used for comparison. Thus, it is possible to evaluate and correlate current visualization of a given patient with his previous cine fluoroscopic studies. The fact still remains that this form of evaluation remains a visualization and progressive anatomical changes are thus not easily documented. Some attempts have been made in grading the morphological appearance of these organs and following the changes of the grading as a function of time and disease. This has proven very unsatisfactory due to the variability of grading between different observers. In our earlier attempts in this area, a complex library of shapes of each anatomical landmark was constructed and stored on a computer. Thus, a review could be made on any patients by asking the computer graphics program to reconstruct a primitive image from the interpretive codes. This proved very unsatisfactory except in the simplest cases due to a lack of quantitative and dynamically obtained data. At that point, it becomes clear that other avenues approximating more closely the realities of the X-ray cine should be sought and coded.

(c) Rationale.

The capability and flexibility of a high data rate computer in the processing of urologically significant radiographic film would provide a medium for the application of sophisticated quantification